Response in which they elected, with traverse, a group of claims that was a modification of Group II prepared by the Examiner. The inventive group of claims elected for prosecution by Applicants reads as follows:

> Claims 1-26, 28 and 29, drawn to compounds and compositions of formula I, and a method for treatment of a disease or disorder, wherein R1 is a saturated, unsubstituted hydrocarbon chain having from 2 to 30 carbon atoms, R2 is phospholipid head group, and D is indomethacin, classified in various classes and subclasses.

In this Supplemental Preliminary Amendment, Applicants have now amended the specification and claims 10 and 20 in order to correct certain inaccuracies and typographical errors. Claim 2 has also been amended in order to more accurately describe the species claimed herein, and support for this amendment to claim 2 can be found at page 19, lines 14-16. Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment, entitled "Version of Amendments With Markings to Show Changes Made".

If the Examiner has any questions or concerns regarding this amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number set forth below.

Respectfully submitted,
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Serial No.: 09/856,009
Filed: May 16, 2001

VERSION OF AMENDMENTS WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION

The paragraph beginning at page 2, line 29:

Diclofenac [(o-[(2,6-dichlorophenyl)amino]phenylacetate)] ([o-[(2,6-dichlorophenyl)amino]phenyl]acetate) is a non-steroidal anti-inflammatory drug of the phenylacetic acid class. When given orally the absorption of diclofenac is rapid and complete. It binds extensively to plasma albumin. Substantial concentrations of drug are attained in synovial fluid, which is the proposed site of action of the NSAIDs. Diclofenac is a potent inhibitor of prostaglandin synthesis and has also been shown to inhibit interleukin-1 (IL-1β) and tumor necrosis factor alpha (TNF-α), involved in osteoarthritis. Gastrointestinal complications such as ulceration and intolerance are the most common adverse effect of diclofenac. Renal dysfunction and hypersensitivity reactions also occur. Many patients with rheumatic disorders have some degree of renal function impairment and are especially susceptible to the induction of renal failure by NSAIDs.

The paragraph beginning at page 6, line 22:

Most preferred compounds according to the invention are:

[1-Stearoyl-2-{3-[2'-(2",6"-dichloroanilino)phenylacetamido]propanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{3-[2-(2,6-dichloroanilino)phenylacetamido]propanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{4-[2'-(2",6"-dichloroanilino)phenylacetamido]butanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{4-[2-(2,6-dichloroanilino)phenylacetamido]butanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{5-[2'-(2",6"-dichloroanilino)phenylacetamido]valeroyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{5-[2-(2,6-dichloroanilino)phenylacetamido]valeroyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{6-[2'-(2",6"-dichloroanilino)phenylacetamido]hexanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{6-[2-(2,6-dichloroanilino)phenylacetamido]hexanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{8-[2'-(2",6"-dichloroanilino)phenylacetamido]octanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{8-[2-(2,6-dichloroanilino)phenylacetamido]octanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{12-[2'-(2",6"-dichloroanilino)phenylacetamido]dodecanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{12-[2-(2,6-dichloroanilino)phenylacetamido]dodecanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{3-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido] propanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{3-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido] propanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{4-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido] butanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{4-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido] butanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{5-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido] valeroyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{5-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido] valeroyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{6-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido] hexanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{6-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido] hexanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{8-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido] octanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{8-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido] octanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{3-[α-methyl-4-(2-methylpropyl)benzeneacetamido]propanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{3-[α-methyl-4-(2-methylpropyl)benzeneacetamido] propanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{6-[α-methyl-4-(2-methylpropyl)benzeneacetamido]hexanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{6-[α-methyl-4-(2-methylpropyl)benzeneacetamido] hexanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{3-[(S)-6-methoxy-α-methyl-2-naphtaleneacetamido]propanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{3-[(S)-6-methoxy-α-methyl-2-naphtaleneacetamido] propanoyl}-sn-glycero-3-phosphocholine,
[1-Stearoyl-2-{4-[(S)-6-methoxy-α-methyl-2-naphtaleneacetamido]butanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{4-[(S)-6-methoxy-α-methyl-2-naphtaleneacetamido] butanoyl}-sn-glycero-3-phosphocholine,
[1-Stearoyl-2-{6-[(S)-6-methoxy-α-methyl-2-naphtaleneacetamido]hexanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{6-[(S)-6-methoxy-α-methyl-2-naphtaleneacetamido] hexanoyl}-sn-glycero-3-phosphocholine, and
[1-Stearoyl-2-{4-[2-(6-methoxynaphtyl)acetamido]butanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{4-[2-(6-methoxynaphtyl)acetamido]butanoyl}-sn-glycero-3-phosphocholine.

The paragraph beginning at page 10, line 11:

Fig. 1 depicts body weight changes (%) of rats treated with multiple per os gavage of either vehicle (open circles), 10 mg/kg diclofenac (DCF, filled circles), 30 mg/kg [1-Stearoyl-2-{4-[2'-(2",6"-dichloroanilino)phenylacetamido]butanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{4-[2-(2,6-dichloroanilino)phenylacetamido]butanoyl}-sn-glycero-3-phosphocholine (denoted DP-DCF; Z=3; filled squares) or 30 mg/kg [1-Stearoyl-2-{6-[2'-(2",6"-dichloroanilino) phenylacetamido] hexanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{6-[2-(2,6-dichloroanilino)phenylacetamido] hexanoyl}-sn-glycero-3-phosphocholine (denoted DP-DCF; Z=5; filled triangles).

The paragraph beginning at page 19, line 8:

Any blocking group that reacts with the functional moiety X to mask its reactive function and is readily removable after coupling [,] may be employed. Reagents suitable for use as protecting groups are well known to those skilled in the art and include, but are not limited to, the following: benzyl [chloromate] chloroformate, [benzyloxycarbonate] dibenzyl dicarbonate (for NH2 or NH protection), benzyloxymethyl chloride, dihydropyran (for OH protection), diphenylcarbinol, trimethylacetamidocarbinol (for SH protection) and methoxymethyl chloride (for COOH protection).

The paragraph beginning at page 21, line 1:

A particular scheme for the synthesis of compounds of the invention is outlined in Scheme I. This scheme is exemplified below, in Examples 1 to 5, by the detailed description of the synthesis of specific lipid derivatives of diclofenac [(o-(2,6-dichloroanilino)phenyl acetic acid)] ([o-(2,6-dichloroanilino)phenyl]acetic acid), indomethacin, (1-(p-chlorobenzoyl)-5-methoxy-2-methyl-3-indolylacetic acid), ibuprofen (2-(4-isobutylphenyl)propionic acid), naproxen (d-2-(6-methoxy-2-naphthyl)pro-pionic acid) and 6-methoxy-2-naphthylacetic acid conjugated to phosphatidylcholine. This synthesis is a six-stage process: The first stage is protection of the functional group on the linker, in this case the amino group of an amino acid. The second stage is preparation of anhydride of this protected amino acid. The third stage is the formation of lipid derivative comprising the protected amino acid and a lyso-lecithin. The removal of the protecting group to yield the amino acid lipid conjugate is carried out in the fourth and fifth stages. Linking of the corresponding drug, in these particular examples, diclofenac, indomethacin, ibuprofen, naproxen or 6-methoxy-2-naphthylacetic acid to [1-acyl-2-(n-amino)acyl-sn-glycero-3-phosphatidylcholine] 1-acyl-2-(n-aminoacyl)-sn-glycero-3-phosphocholine is realized in the last stage.

The heading at page 26, lines 8-9:

[*3-(Carbobenzyloxyamino)propanoic*] *3-(Benzyloxycarbonylamino)propanoic acid.* C_6H_5-CH_2-O-C(O)-NH-CH_2-CH_2-COOH.

The heading at page 26, line 13:

[*4-(Carbobenzyloxyamino)butanoic*] *4-(Benzyloxycarbonylamino)butanoic acid.* $C_6H_5CH_2$-O-C(O)-NH-$(CH_2)_3$-COOH.

The heading at page 26, line 17:

[*5-(Carbobenzyloxyamino)valeric*] *5-(Benzyloxycarbonylamino)valeric acid.* $C_6H_5CH_2$-O-C(O)-NH-$(CH_2)_4$-COOH.

The heading at page 26, line 21:

[6-(Carbobenzyloxyamino)hexanoic] 6-(Benzyloxycarbonylamino)hexanoic acid. $C_6H_5CH_2$-O-C(O)-NH-$(CH_2)_5$-COOH.

The heading at page 26, line 25:

[8-(Carbobenzyloxyamino)octanoic] 8-(Benzyloxycarbonylamino)octanoic acid. $C_6H_5CH_2$-O-C(O)-NH-$(CH_2)_7$-COOH.

The heading at page 27, lines 1-2:

[12-(Carbobenzyloxyamino)dodecanoic] 12-(Benzyloxycarbonylamino)dodecanoic acid. $C_6H_5CH_2$-O-C(O)-NH-$(CH_2)_{11}$-COOH.

The paragraph beginning at page 27, line 9:

The solution of corresponding Z-aminoacid produced at stage 1 (0.05 mol) in freshly distilled dichloromethane (25 ml) is introduced, under an inert atmosphere of argon, into double-neck round-bottom flask (100 ml) equipped with magnetic stirrer and dropped funnel. A solution of dicyclohexylcarbodiimide (0.0325 mol) in 25 ml of freshly distilled dichloromethane, also under argon, is added drop wise, with stirring, to the solution of Z-amino acid. After 20 min of stirring, the obtained precipitate of urea is filtered and the solution evaporated under vacuum. The crude residue is washed with hexane (2X 20 ml) and then dried in vacuum.

The heading at page 27, line 22:

Anhydride of [Z-(3-amino)propanoic] 3-(Z-amino)propanoic acid.

The heading at page 27, line 26:

Anhydride of [Z-(4-amino)butanoic] 4-(Z-amino)butanoic acid.

The heading at page 27, line 30:

Anhydride of [Z-(5-amino)valeric] 5-(Z-amino)valeric acid.

The heading at page 28, line 3:

Anhydride of [*Z-(6-amino)hexanoic*] *6-(Z-amino)hexanoic acid.*

The heading at page 28, line 7:

Anhydride of [*Z-(8-amino)octanoic*] *8-(Z-amino)octanoic acid.*

The heading at page 28, line 11:

Anhydride of [*Z-(12-amino)dodecanoic*] *12-(Z-amino)dodecanoic acid.*

The heading and paragraph beginning at page 28, line 16:

Stage 3. Preparation of [1-acyl-2-(Z-amino)acyl-sn-glycero-3-phosphotidylcholine] 1-acyl-2-(Z-aminoacyl)-sn-glycero-3-phosphocholine.

The anhydride of the corresponding Z-amino acid, 0.01 mol dissolved in 150 ml of freshly distilled chloroform, is introduced, under an inert atmosphere of argon, into a single-neck round-bottom flask (250 ml) equipped with a magnetic stirrer. To this solution 0.01 mol (1.22 g) 4-(dimethylamino)pyridine (DMAP) in 25 ml chloroform is added, followed by addition of a suspension of 0.0056 moles lyso-lecithin in 50 ml of chloroform. The reaction mixture is vigorously stirred for 3-5 hours at room temperature. The lyso-lecithin dissolves and reaction mixture becomes transparent after about 2 hours of stirring. The reaction is monitored by TLC using silica gel 60 on aluminum sheet, the eluent is chloroform:methanol:water, 65:35:5, the indicator is a spray of the composition: 4-methoxybenzaldehyde (10 ml), absolute ethanol (200 ml), 98% sulfuric acid (10 ml) and glacial acetic acid (2 ml). The chromatogram is sprayed with the indicator followed by charring with hot air at 150°C. The reaction is assumed to be complete and stopped when all the lyso-lecithin has disappeared. The reaction mixture is then transferred into a separating funnel and washed with a solution of 1% HCl (3x 50 ml), then with saturated solution of sodium bicarbonate (3x 50 ml) and finally with water (3x 50 ml). The obtained product in the organic solution is dried over sodium sulfate and then filtered. The solvent is evaporated at 30°C in [vacuo] a vacuum and the residue is washed with hexane and left to dry overnight under vacuum. The resulted molecule [1-acyl-2-(Z-amino)acyl-sn-glycero-3-phosphatidylcholine] 1-acyl-2-(Z-aminoacyl)-sn-glycero-3-phosphocholine is the main product

of the reaction.

The paragraph beginning at page 29, line 9:

The second product of the reaction is the Z-amino acid. In order to increase the yield of this product, it is back-extracted from reaction mixture as follows: The sodium bicarbonate aqueous fractions are collected and combined and then acidified by 3 N HCl to pH 1. The Z-amino acid is extracted by chloroform (2x 50 ml). The chloroform extracts were combined, washed once with water and dried over sodium sulfate for 30 min with stirring. The sodium sulfate is removed by filtration, and the chloroform evaporated. Subsequently, the residue is washed with hexane and dried over P_2O_5 in [vacuo] a vacuum.

The heading at page 29, lines 23-24:

[1-Stearoyl-2-[3'-(carbobenzyloxyamino)]propanoyl-sn-glycero-3-phosphotidyl choline] 1-Stearoyl-2-[3-(benzyloxycarbonylamino) propanoyl]-sn-glycero-3-phosphocholine.

The heading at page 30, lines 1-2:

[1-Stearoyl-2-[4'-(carbobenzyloxyamino)]butanoyl-sn-glycero-3-phosphotidyl choline] 1-Stearoyl-2-[4-(benzyloxycarbonyl amino) butanoyl]-sn-glycero-3-phosphocholine.

The heading at page 30, lines 9-10:

[1-Stearoyl-2-[5'-(carbobenzyloxyamino)]valeroyl-sn-glycero-3-phosphotidyl choline] 1-Stearoyl-2-[5-(benzyloxycarbonylamino) valeroyl]-sn-glycero-3-phosphocholine.

The heading at page 30, lines 17-18:

[1-Stearoyl-2-[6'-(carbobenzyloxyamino)]hexanoyl-sn-glycero-3-phosphotidyl choline] 1-Stearoyl-2-[6-(benzyloxycarbonylamino) hexanoyl]-sn-glycero-3-phosphocholine.

The heading at page 30, lines 25-26:

[1-Stearoyl-2-[8'-(carbobenzyloxyamino)]octanoyl-sn-glycero-3-phosphotidyl choline] 1-Stearoyl-2-[8-(benzyloxycarbonylamino) octanoyl]-sn-glycero-3-phosphocholine.

The heading at page 31, lines 2-3:

[1-Stearoyl-2-[12'-(carbobenzyloxyamino)]dodecanoyl-sn-glycero-3-phosphotidylcholine] 1-Stearoyl-2-[12-(benzyloxycarbonylamino)-dodecanoyl]-sn-glycero-3-phosphocholine.

The paragraph beginning at page 31, line 11:

The obtained [1-stearoyl-2-(carbobenzyloxyamino)acyl-3-phosphotidylcholine] 1-stearoyl-2-[(benzyloxycarbonylamino)acyl]-3- phosphocholine (0.0025 mol) is dissolved in a mixture of 100 ml methanol and 5 ml acetic acid. The solution is introduced into round bottom double neck flask (200 ml) equipped with a magnetic stirrer, under an atmosphere of argon. Pd/C (0.5 g) is added to the solution and hydrogen is blown through the reaction mixture for 4 hours. The reaction proceeding is monitored by TLC analysis under the following conditions: silica gel 60 on aluminum sheet, eluent is the mixture of chloroform/methanol/water (65:35:5, v/v), indicator is a spray of the composition: p-methoxybenzaldehyde (10 ml), absolute ethanol (200 ml), 98% sulfuric acid (10 ml) and glacial acetic acid (2 ml). The chromatogram is sprayed with the indicator and then charred using hot air at 100-150^{0}C.

The paragraph beginning at page 31, line 22:

The reaction assumed to be complete and hydrogenation is stopped after all corresponding [1-stearoyl-2-carbobenzyloxyaminoacyl-sn-glycero-phosphatidylcholine] 1-stearoyl-2-[(benzyloxycarbonylamino)acyl]-sn-glycero-phosphocholine has disappeared. The reaction mixture is then filtered through celete to remove the Pd/C, evaporated at 30°C, under vacuum. The crude residue is washed with ether (3x 30 ml) and dried in [vacuo] a vacuum overnight. Conditions of the TLC analysis are the same as indicated above.

The heading at page 31, lines 28-29:

[1-Stearoyl-2-(3-amino)propanoyl-sn-glycero-3-phosphatidylcholine, acetic acid] 1-Stearoyl-2-(3-aminopropanoyl)-sn-glycero-3-phosphocholine, acetate.

The heading at page 32, line 8:

[*1-Stearoyl-2-(4-amino)butanoyl-sn-glycero-3-phosphatidylcholine, acetic acid*] *1-Stearoyl-2-(4-aminobutanoyl)-sn-glycero-3-phosphocholine, acetate.*

The heading at page 32, line 18:

[*1-Stearoyl-2-(5-amino)valeroyl-sn-glycero-3-phosphatidylcholine, acetic acid*] *1-Stearoyl-2-(5-aminovaleryl)-sn-glycero-3-phosphocholine, acetate.*

The heading at page 32, line 28:

[*1-Stearoyl-2-(6-amino)hexanoyl-sn-glycero-3-phosphatidylcholine, acetic acid*] *1-Stearoyl-2-(6-aminohexanoyl)-sn-glycero-3-phosphocholine, acetate.*

The heading at page 33, line 7:

[*1-Stearoyl-2-(8-amino)octanoyl-sn-glycero-3-phosphatidylcholine, acetic acid*] *1-Stearoyl-2-(8-aminooctanoyl)-sn-glycero-3-phosphocholine, acetate.*

The heading at page 33, lines 17-18:

[*1-Stearoyl-2-(12-amino)dodecanoyl-sn-glycero-3-phosphatidylcholine, acetic acid*] *1-Stearoyl-2-(12-aminododecanoyl)-sn-glycero-3-phosphocholine, acetate.*

The heading and paragraph beginning at page 33, line 27-28:

Stage 5. Preparation of free [1-acyl-2-[n(amino)acyl-sn-glycero-3-phosphatidylcholine] 1-acyl-2-[n-(aminoacyl)-sn-glycero-3-phosphocholine

The solution of acetic acid and the corresponding [1-acyl-2-[n-aminoacyl-sn-glycero-3-phosphatidylcholine] 1-acyl-2-[n-(aminoacyl)-sn-glycero-3-phosphocholine complex (1.36 mmol) in methylene chloride (30 ml) is introduced into a single neck round bottom flask (150 ml) equipped with a magnetic stirrer. Triethylamine (0.3 ml, 3 mmol) is added to this solution. The resulting reaction mixture is stirred at room temperature for 30 min. During this procedure the free 2-amino-acyl lipid is formed. The reaction solution with the obtained free 2-amino-acyl lipid is used for the following synthesis without any additional processing.

The heading at page 34, lines 7-8:

Stage 6. Preparation of [1-acyl-2-n(arylacetamido)acyl-sn-glycero-3-phosphatidylcholine]

1-acyl-(2-n-arylacetamidoacyl)-sn-glycero-3-phosphocholine

The heading at page 35, lines 4-5:

[1-Stearoyl-2-{3-[2'-(2",6"-dichloroanilino)phenylacetamido]propanoyl}-sn- glycero-3-phosphatidylcholine] 1-Stearoyl-2-{3-[2-(2,6-dichloroanilino)phenylacetamido]propanoyl}-sn-glycero-3-phosphocholine.

The heading at page 35, lines 24-25:

[1-Stearoyl-2-{4-[2'-(2",6"-dichloroanilino)phenylacetamido]butanoyl}-sn- glycero-3-phosphatidylcholine] 1-Stearoyl-2-{4-[2-(2,6-dichloroanilino)phenylacetamido]butanoyl}-sn-glycero-3-phosphocholine.

The heading at page 36, lines 12-13:

[1-Stearoyl-2-{5-[2'-(2",6"-dichloroanilino)phenylacetamido]valeroyl}-sn- glycero-3-phosphatidylcholine] 1-Stearoyl-2-{5-[2-(2,6-dichloroanilino)phenylacetamido]valeryl}-sn-glycero-3-phosphocholine.

The heading at page 37, lines 1-2:

[1-Stearoyl-2-{6-[2'-(2",6"-dichloroanilino)phenylacetamido]hexanoyl}-sn- glycero-3-phosphatidylcholine] 1-Stearoyl-2-{6-[2-(2,6-dichloroanilino)phenylacetamido]hexanoyl}-sn-glycero-3-phosphocholine.

The heading at page 37, lines 13-14:

[1-Stearoyl-2-{8-[2'-(2",6"-dichloroanilino)phenylacetamido]octanoyl}-sn- glycero-3-phosphatidylcholine] 1-Stearoyl-2-{8-[2-(2,6-dichloroanilino)phenylacetamido]octanoyl}-sn-glycero-3-phosphocholine.

The heading at page 38, lines 10-11:

[1-Stearoyl-2-{12-[2'-(2",6"-dichloroanilino)phenylacetamido]dodecanoyl}-sn- glycero-3-phosphatidylcholine] 1-Stearoyl-2-{12-[2-(2,6-dichloroanilino)phenylacetamido]dodecanoyl}-sn- glycero-3-phosphocholine.

The heading at page 39, lines 15-16:

[1-Stearoyl-2-{3-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl-3- indolylacetamido]propanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{3-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl-3-indolylacetamido]propanoyl}-sn- glycero-3-phosphocholine.

The heading at page 40, lines 8-9:

[1-Stearoyl-2-{4-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl-3-indolylacetamido]butanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{4-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl-3-indolylacetamido]butanoyl}-sn- glycero-3-phosphocholine.

The heading at page 41, lines 1-2:

[1-Stearoyl-2-{5-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl-3-indolylacetamido]valeroyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{5-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl-3-indolylacetamido]valeryl}-sn-glycero-3-phosphocholine.

The heading at page 41, lines 18-19:

[1-Stearoyl-2-{6-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl-3-indolylacetamido]hexanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{6-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl-3-indolylacetamido]hexanoyl}-sn- glycero-3-phosphocholine.

The heading at page 42, lines 14-15:

[1-Stearoyl-2-{8-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl-3-indolylacetamido]octanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{8-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl-3-indolylacetamido]octanoyl}-sn- glycero-3-phosphocholine.

The heading at page 43, lines 19-20:

[1-Stearoyl-2-{3-[α-methyl-4-(2-methylpropyl)benzeneacetamido]propanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{3-[α-methyl-4-(2-methylpropyl)benzeneacetamido] propanoyl}-sn-glycero-3-phosphocholine.

The heading at page 44, lines 9-10:

[1-Stearoyl-2-{6-[α-methyl-4-(2-methylpropyl)benzeneacetamido]hexanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{6-[α-methyl-4-(2-methylpropyl)benzeneacetamido] hexanoyl}-sn-glycero-3-phosphocholine.

The heading at page 45, lines 15-16:

[1-Stearoyl-2-{3-[(S)-6-methoxy-α-methyl-2-naphtaleneacetamido]propanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{3-[(S)-6-methoxy-α-methyl-2-naphtaleneacetamido] propanoyl}-sn-glycero-3-phosphocholine.

The heading at page 46, lines 7-8:

[1-Stearoyl-2-{4-[(S)-6-methoxy-α-methyl-2-naphtaleneacetamido]butanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{4-[(S)-6-methoxy-α-methyl-2-naphtaleneacetamido] butanoyl}-sn-glycero-3-phosphocholine.

The heading at page 47, lines 1-2:

[1-Stearoyl-2-{6-[(S)-6-methoxy-α-methyl-2-naphtaleneacetamido]hexanoyl}-sn-glycero-3-phosphatidyl] 1-Stearoyl-2-{6-[(S)-6-methoxy-α-methyl-2-naphtaleneacetamido]hexanoyl}-sn-glycero-3-phosphocholine.

The heading at page 48, lines 10-11:

[1-Stearoyl-2-{4-[2-(6-methoxynaphtyl)acetamido]butanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{4-[2-(6-methoxynaphtyl)acetamido]butanoyl}-sn-glycero-3-phosphocholine.

The paragraph beginning at page 51, line 23:

The ability of the compounds of the invention to be cleaved to yield free diclofenac, was studied in vitro in homogenates of rat brain and liver. Two compounds were tested: the prodrug [1-Stearoyl-2-{4-[2'-(2",6"-dichloroanilino)-phenylacetamido]butanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{4-[2-(2,6-dichloroanilino)-phenylacetamido]butanoyl}-sn-glycero-3-phosphocholine (DP-DFC; Z=3), and the compound [1-Stearoyl-2-{3-[2'-(2",6"-dichloroanilino) -phenylacetamido]propanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{3-[2-(2,6-dichloroanilino) -phenylacetamido]propanoyl}-sn-glycero-3-phosphocholine (DP-DFC; Z=2), comprising, respectively, a bridging group having a total of 4 and 3 carbon atoms.

The paragraph beginning at page 53, line 20:

Male Sprague-Dawley rats weighing 250-280 g were kept under standard conditions for an acclimatization period of one week with food and water supplied ad lib. The rats were administered with commercial diclofenac (DCF; Sigma, USA) or with equivalent doses of [1-Stearoyl-2-{4-[2'-(2",6"-dichloroanilino)-phenylacetamido]butanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{4-[2-(2,6-dichloroanilino)-phenylacetamido]butanoyl}-sn-glycero-3-phosphocholine (DP-DCF; Z=3) or [1-Stearoyl-2-{6-[2'-(2",6"-dichloroanilino)-phenylacetamido]hexanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{6-[2-(2,6-dichloroanilino)-phenylacetamido]hexanoyl}-sn-glycero-3-phosphocholine (DP-DCF; Z=5), p.o. by gavage daily for 14 days. Animals treated with the vehicle solution alone serve as control group.

IN THE CLAIMS

2. (Amended) The compound according to claim 1, wherein the conjugated residue of the nonsteroidal anti-inflammatory drug [derivative] is pharmacologically inactive.

10. (Amended) The compound according to claim 1 selected from the group consisting of:

[1-Stearoyl-2-{3-[2'-(2",6"-dichloroanilino)phenylacetamido]propanoyl}-sn-glycero-3-

phosphatidylcholine] 1-Stearoyl-2-{3-[2-(2,6-dichloroanilino)phenylacetamido]propanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{4-[2'-(2",6"-dichloroanilino)phenylacetamido]butanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{4-[2-(2,6-dichloroanilino)phenylacetamido]butanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{5-[2'-(2",6"-dichloroanilino)phenylacetamido]valeroyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{5-[2-(2,6-dichloroanilino)phenylacetamido]valeroyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{6-[2'-(2",6"-dichloroanilino)phenylacetamido]hexanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{6-[2-(2,6-dichloroanilino)phenylacetamido]hexanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{8-[2'-(2",6"-dichloroanilino)phenylacetamido]octanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{8-[2-(2,6-dichloroanilino)phenylacetamido]octanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{12-[2'-(2",6"-dichloroanilino)phenylacetamido]dodecanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{12-[2-(2,6-dichloroanilino)phenylacetamido]dodecanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{3-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido]propanoyl} sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{3-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido]propanoyl} sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{4-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido]butanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{4-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido]butanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{5-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido]valeroyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{5-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido]valeroyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{6-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido]hexanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{6-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido]hexanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{8-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido]octanoyl}-

sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{8-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido]octanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{3-[α-methyl-4-(2-methylpropyl)benzeneacetamido] propanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{3-[α-methyl-4-(2-methylpropyl)benzeneacetamido] propanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{6-[α-methyl-4-(2-methylpropyl)benzeneacetamido] hexanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{6-[α-methyl-4-(2-methylpropyl)benzeneacetamido] hexanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{3-[(S)-6-methoxy-α-methyl-2-naphtaleneacetamido] propanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{3-[(S)-6-methoxy-α-methyl-2-naphtaleneacetamido] propanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{4-[(S)-6-methoxy-α-methyl-2-naphtaleneacetamido] butanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{4-[(S)-6-methoxy-α-methyl-2-naphtaleneacetamido] butanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{6-[(S)-6-methoxy-α-methyl-2-naphtaleneacetamido] hexanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{6-[(S)-6-methoxy-α-methyl-2-naphtaleneacetamido] hexanoyl}-sn-glycero-3-phosphocholine, and

[1-Stearoyl-2-{4-[2-(6-methoxynaphtyl)acetamido]butanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{4-[2-(6-methoxynaphtyl)acetamido]butanoyl}-sn-glycero-3-phosphocholine.

20. (Amended) The pharmaceutical composition according to claim 11, wherein said compound of the general formula I is selected from the group consisting of:

[1-Stearoyl-2-{3-[2'-(2",6"-dichloroanilino)phenylacetamido]propanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{3-[2-(2,6-dichloroanilino)phenylacetamido]propanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{4-[2'-(2",6"-dichloroanilino)phenylacetamido]butanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{4-[2-(2,6-dichloroanilino)phenylacetamido]butanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{5-[2'-(2",6"-dichloroanilino)phenylacetamido]valeroyl}-sn-glycero-3-

phosphatidylcholine] 1-Stearoyl-2-{5-[2-(2,6-dichloroanilino)phenylacetamido]valeroyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{6-[2'-(2",6"-dichloroanilino)phenylacetamido]hexanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{6-[2-(2,6-dichloroanilino)phenylacetamido]hexanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{8-[2'-(2",6"-dichloroanilino)phenylacetamido]octanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{8-[2-(2,6-dichloroanilino)phenylacetamido]octanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{12-[2'-(2",6"-dichloroanilino)phenylacetamido]dodecanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{12-[2-(2,6-dichloroanilino)phenylacetamido]dodecanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{3-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido] propanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{3-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido] propanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{4-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido]butanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{4-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido]butanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{5-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido]valeroyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{5-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido]valeroyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{6-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido]hexanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{6-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido]hexanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{8-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido]octanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{8-[1-(p-chlorobenzoyl)-5-methoxy-2-methyl indolylacetamido]octanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{3-[α-methyl-4-(2-methylpropyl)benzeneacetamido]propanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{3-[α-methyl-4-(2-methylpropyl) benzeneacetamido]propanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{6-[α-methyl-4-(2-methylpropyl)benzeneacetamido] hexanoyl}-sn-glycero-

3-phosphatidylcholine] 1-Stearoyl-2-{6-[α-methyl-4-(2-methylpropyl)benzeneacetamido] hexanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{3-[(S)-6-methoxy-α-methyl-2-naphtaleneacetamido]propanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{3-[(S)-6-methoxy-α-methyl-2-naphtaleneacetamido]propanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{4-[(S)-6-methoxy-α-methyl-2-naphtaleneacetamido]butanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{4-[(S)-6-methoxy-α-methyl-2-naphtaleneacetamido] butanoyl}-sn-glycero-3-phosphocholine,

[1-Stearoyl-2-{6-[(S)-6-methoxy-α-methyl-2-naphtaleneacetamido] hexanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{6-[(S)-6-methoxy-α-methyl-2-naphtaleneacetamido] hexanoyl}-sn-glycero-3-phosphocholine, and

[1-Stearoyl-2-{4-[2-(6-methoxynaphtyl)acetamido]butanoyl}-sn-glycero-3-phosphatidylcholine] 1-Stearoyl-2-{4-[2-(6-methoxynaphtyl)acetamido]butanoyl}-sn-glycero-3-phosphocholine.